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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/518,501 03/03/00 ERION

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EXAMINER

HM12/0823

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MCKENZIE T	
ART UNIT	PAPER NUMBER

1624  
DATE MAILED:

08/23/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

## Office Action Summary

Application No.

09/518,501

Applicant(s)

ERION ET AL.

Examiner

Thomas McKenzie Ph.D.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 July 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-157, 161 and 163-165 is/are pending in the application.
- 4a) Of the above claim(s) 19, 47, 58-149, 161, 163 and 164 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-18, 20-46, 48-57, 150-157 and 165 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. This action is in response to an election filed on 7/23/01. There are one hundred sixty-one claims pending and sixty-four are under consideration. Claims 1-16, 17-46, 48-57, and 165 are compound claims. Claims 150-157 are method of preparation claims. Applicants have withdrawn claims 158-160 and 162. This is the first action on the merits. The application concerns some cyclic phosphate amides and preparations thereof.

#### *Election/Restrictions*

2. In the previous office action, the Examiner erroneously indicated that claim 47 was a linking claim. It is drawn to compounds where both Y = nitrogen. Thus, it is a member of Group II. Applicant's election without traverse of Groups I and XIX in Paper No. 8 is acknowledged. Claims 19, 47, and 161 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

Applicants were asked to select one group of uses from Groups III-XVIII but failed to do so. To quote from the MPEP §806.05(h) "Product and Process of Using a product and a process of using the product can be shown to be distinct inventions if ... ". This says a single process, not Applicants' sixteen separate

processes. The Utility Guidelines have been changed to require one specific utility, consistent with 37 CFR 1.1475 and PCT Rule 13.2. In addition, 37 CFR 1.141(a) provides that two or more independent and distinct inventions may not be claimed in one application. Thus, claims 58-149, 163, and 164 are withdrawn from consideration.

3. Claims 1-1620-46, 48-57, 150-157, and 165 are rejected on the grounds as being drawn to an improper Markush group *In re Harnisch* 206 USPQ 300. The claimed compounds, compositions, and methods that employ them present a variable core. Deletion of non-elected subject matter obviates this rejection. The Examiner suggests deleting any reference to both Y = nitrogen.

#### ***Information Disclosure Statement***

4. The information disclosure statement filed 6/11/01 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. None of the references listed are with the application. It has been placed in the application file, but the information referred to therein has not been considered.

### ***Claim Objections***

5. Claims 152, 155, and 156 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicants have the proviso in claim 1 that “V, Z, W, W’ are not all -H”. Thus, all the molecules containing the fragment Y-CH(V)CH(Z)-CW(W’)-Y must be chiral and no subject matter is excluded by the requirement “is chiral”.

### ***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “fused to an aryl group at the beta and gamma position to the Y adjacent to V” is confusing. The use of beta and gamma in nomenclature is an archaic usage but art recognized to apply only to claims not rings. The word beta, when applied to rings indicates stereochemistry not position. The word gamma has no stereo chemical meaning in rings. The

word beta means up in steroids but down in carbohydrates. Since the cyclic group formed by V and Z is neither a steroid nor a carbohydrate, what do Applicants intend? Does the phrase "beta and gamma position" refer to the aryl ring, the cyclic group containing V and Z, or the ring containing the Y? If the latter, does one count clockwise or counterclockwise from the Y? If Applicants are intending the fusion point to be in the cyclic group containing V and Z, how does one count from Y? What does one do at ring junctures?

7. Claims 1-18, 20-46, 48-57, 150-157, and 165 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In line 18, page 127 Applicants claim "acyloxy", in line 11, page 128 Applicants claim "acyloxyalkyl", and in line 12, page 128 Applicants' claim "lower acyl". The accepted meaning of the term "acyl" is "any acid substituent with the OH group removed". The term acyl is indefinite. Does this embrace the acids of sulfur and phosphorus? How is the acyl group attached? Is it through the central atom of the acid group or through some other carbon atom? What is the specific stem, i.e. if acyl is  $RC(O)$ , what is R? In acyl groups derived from carboxylic acids, does the adjective "lower" include the carbonyl carbon atom?

8. Claims 1-3, 7, 9-18, 20-46, 48-53, 150-157, and 165 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase in lines 16-17, page 128, "M is selected from ... but is not an FBPase inhibitor" is indefinite for three reasons. Firstly, it is unclear if M must itself contain phosphorus. Secondly, what do Applicants intend by "biologically active agent? How active and active as what? Thirdly, what is FBP or FBPase?

9. Claims 1-3, 7, 9-18, 20-46, 48-53, 150-157, and 165 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase in lines 20-21, page 128 "M is not -NH(lower alkyl), -N(lower alkyl)<sub>2</sub>" is indefinite. M must be biologically active. Are NH<sub>2</sub>(lower alkyl) or HN(lower alkyl)<sub>2</sub> biologically active? If not, the proviso excluded something that is not present. The nitrogen mustards excluded (lower alkyl halide) are toxins, thus meet the test of biologically active.

10. Claims 1-18, 20-46, 48-57, 150-157, and 165 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In line 23, page 128 and elsewhere, Applicants claim "prodrug". The word

"prodrug" is indefinite. The issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrugs" are molecules whose structure lie outside the subject matter of claim 1, but upon metabolism in the body are converted to active compounds falling within the structural scope of claim 1. The claim describes the function intended but provides no specific structural guidance to what constitutes a "prodrug". The compounds of formula (I) are described in the specification as prodrugs. Are Applicants' claiming prodrugs of prodrugs or does the word in line 23 simply reinforce the nature of the compounds of formula (I)?

11. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What is "TS"?

12. Claims 4-6, 8, 54, 55, and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What are the compounds whose abbreviations are given? They are not named in the specification and these are not recognized names in the art of organic chemistry. None of these are listed in Hawley's "Condensed Chemical Dictionary". For example, search of Chemical Abstracts reveals seven listings for "LdC", one



hundred thirty-one listings for “LdT”, seventeen listings for “araA”, two different listings for “AZT”, and eight listings for “PMEA”. Which ones do Applicants intend? Search of Chemical Abstracts for “TFT” fails to find a compound with this name. If any of the names are registered trademarks, then the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. The Examiner suggests using either structural formulas, CA names, or art-recognized complete names to indicate what Applicants intend. What ever choices Applicants make must be supported in the specification.

13. Claims 38, 42, 46, and 165 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrases “said prodrugs” and “the prodrug” are indefinite. What are the structures being claimed? Claim 20 does not contain the word. Claim 1 appears to contain both compounds of formula (I) and prodrugs of the compounds of formula (I). Since

the compounds of formula (I) are prodrugs, which ones are the “said prodrugs” or “the prodrug”?

14. Claim 150 provides for transforming “a compound drug having a  $-\text{PO}_3^{2-}$  ...”, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. All the word “transforming” does is delineate which molecules are starting materials and which are products. What chemical reactions are being claimed?

Claim 150 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

15. Claims 154-157 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “oxidizing agent” is indefinite. Pauling’s “General Chemistry” on page 248 says, “[a]n atom, molecule,

or ion which takes up electrons is called an oxidizing agent". "The Condensed Chemical Dictionary" defines "oxidizing material" as "any compound that spontaneously evolves oxygen..". What are the structures of the reagents, whose use Applicants claim? The Examiner suggests listing the "oxidizing agents" intended. Whatever choices are made must be supported by the specification.

16. Claim 156 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "using a chiral alcohol" is indefinite for two reasons. Firstly, Claim 156 provides for the use of "a chiral alcohol", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Secondly, what amino alcohol does this refer? Is it the amino alcohol  $\text{HY-CH(V)CH(Z)-CW(W')-YH}$ ? Is it present somewhere else in the molecule? Is it an auxiliary in solution or attached to a reagent but not incorporated into the final product?

Claim 156 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim

under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7, 9-18, 20-46, 48-53, 56, 150-157, and 165 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The phrase in lines 16-17, page 128, "M is selected from ... but is not an FBPase inhibitor" lacks written description. Applicants' claims are drawn to any molecule with a specific biological property. What are the structures of these molecules and where in the specification do Applicants teach how to make this potentially limitless structural variety of such molecules? Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claims 1-3, 7, 9-18, 20-46, 48-53, 56, 150-157, and 165. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise. Applicants'

dependant claims, listing the specific diseases treated, do not clarify what is intended here.

Is extensive experimentation required on the part of a potential infringer to determine if his molecule within the limitations of applicants' claim? *In re Kirk and Petrow*, 153 USPQ 48 (CCPA 1967). As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates."

18. Claims 1-18, 20-46, 48-57, 150-157, and 165 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Nowhere in the specification are directions given for preparing the "prodrugs" of the claimed compounds. Since the structures of these "prodrugs" are uncertain, direction for their preparation must be even more unclear.

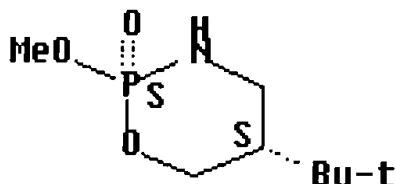
***Claim Rejections - 35 USC § 102***

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

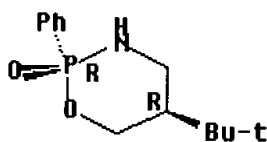
A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 17, 18, 20, and 165 are rejected under 35 U.S.C. 102(b) as being anticipated by Bentrude (J. Am. Chem. Soc. 1986). Two compounds in this reference anticipate Applicants' claims. The compound shown below meets the limitation of formula I with  $R^6$  = hydrogen, Z = tert-butyl, V = W = W' = hydrogen, and M = methoxy. Both methanol and methyl phosphate meet the limitation of biologically active. The compounds are found in the reference in the diagram in the middle of page 6669 and are compounds 8 and 10.

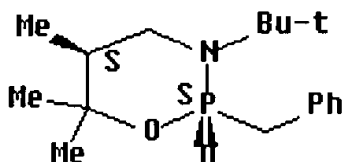


20. Claims 1, 9, 17, 18, 20, 150-152, 154-156, and 165 are rejected under 35 U.S.C. 102(b) as being anticipated by Bentrude (J. Am. Chem. Soc. 1988). Six compounds in this reference anticipate Applicants claims. The compound shown below meets the limitation of formula I with Z = tert-butyl, V = W = W' = hydrogen, and M = phenyl. For all the Examiner knows, phenyl phosphonate is biologically active. The compounds are found in the reference in the diagram on the right side of page 7119 and are compounds 6, 8, 9, 11, and 12. Synthesis is outlined in the first complete paragraph on page 6970.

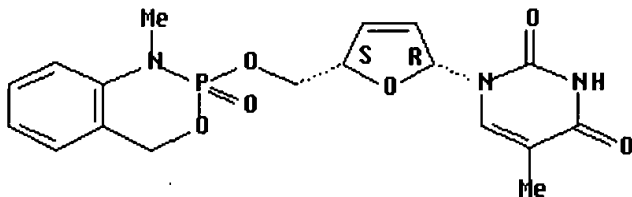


21. Claims 1, 9, 17, 18, 20, 150-157, and 165 are rejected under 35 U.S.C. 102(b) as being anticipated by Denmark (Tetrahedron). The compound shown below meets the limitation of formula I with R<sup>6</sup> = tert-butyl, Z = W = W' = methyl, V = hydrogen, and M = benzyl. For all the Examiner knows, benzyl phosphonate is biologically active. . The compound is found in the reference in

Table 1, page 2193 Table, 3, page 2197, and is compound 1d. Synthesis is outlined in the paragraph spanning pages 2202-2203.



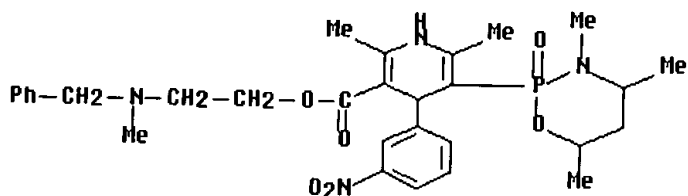
22. Claims 1, 2, 4, 7, 11-13, 17, 18, 20, 21, 29, and 165 are rejected under 35 U.S.C. 102(a) as being anticipated by Lorey (Nucleosides Nucleotides). The compound shown below meets the limitation of formula I with  $R^6$  = methyl,  $Z = V$  = fused benzo,  $W = W'$  = hydrogen, and  $M = d4T$ .



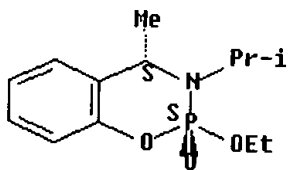
23. Claims 1, 9, 11, 17, 18, 20, and 165 are rejected under 35 U.S.C. 102(b) as being anticipated by Kamikawaji (JP 62-195392 A2). Six compounds in this reference anticipate Applicants' claims. The compound shown below meets the limitation of formula I with  $R^6$  = methyl,  $V = W$  = methyl,  $Z = W'$  = hydrogen, and  $M = 1,4$ -dihydro-2,6-dimethyl-4-(3-nitrophenyl 3-pyridinecarboxylic acid. The



reference teaches that these compounds are useful for circulation disorders. The compound is found in the reference in Table 1-6 on page 822.

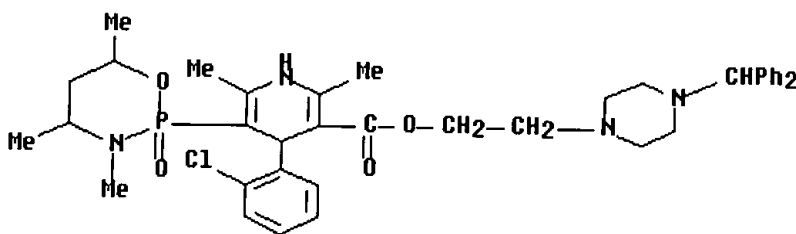


24. Claims 1, 2, 4, 7, 11-13, 17, 18, 20, 21, 29, and 165 are rejected under 35 U.S.C. 102(a) as being anticipated by Yoshikawa (JP 62-249996 A2). The compound shown below meets the limitation of formula I with  $R^6$  = isopropyl, Z = V = fused benzo, W = methyl, W' = hydrogen, and M = ethoxy. Ethanol and ethyl phosphate are certainly biologically active. The compound is found in the reference in the table on page 21. It is compound 85. Other compounds which anticipate Applicants' claims are 81-84, 86, 87, 100-102



25. Claims 1, 2, 9, 11, 12, 13, 17, 18, 20, and 165 are rejected under 35 U.S.C. 102(b) as being anticipated by Akiyama ('303). The compound shown

below meets the limitation of formula I with  $R^6$  = methyl,  $V = W$  = methyl,  $Z = W'$  = hydrogen, and  $M$  = 4-(2-chlorophenyl)-1,4-dihydro-2,6-dimethyl-3-pyridinecarboxylic acid 2-[4-(diphenylmethyl)-1-piperazinyl]ethyl ester. The reference teaches that these compounds are useful for cancer treatment. The compound is found in the reference as the second compound in the Table in column 23. See also claims 3 and 4 of this reference.



### *Conclusion*

26. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for the Examiner is (703) 746-3152. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mukund Shah can be reached on (703) 308-4716. Please direct general

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inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

*Mukund J. Shah*  
**Mukund Shah**  
**Supervisory Patent Examiner**  
**Art Unit 1624**

TCMcK  
August 17, 2001

